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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/828,456	04/06/2001	Stuart B. Levy	PKZ-030	6918

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EXAMINER	
HINES, JANA A	

ART UNIT	PAPER NUMBER
1645	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	09/828,456	LEVY ET AL.	
	Examiner	Art Unit	
	Ja-Na Hines	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on *04 September 2003*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *16-25* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *16-25* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Amendment Entry

1. The amendment filed September 4, 2003 has been entered. The examiner acknowledges the amendment to the specification. Claims 1-15 and 26-28 have been cancelled. Claims 16-24 have been amended. Claims 16-25 are under consideration in this office action.

Withdrawal of Rejections

2. The following rejections have been withdrawn in view of applicants' amendments:

a) The enablement rejection of claims 16-25 under 35 U.S.C. 112, first paragraph;

b) The rejection of claims 16-25 under 35 U.S.C. 112, second paragraph, as being indefinite; and

c) The rejection of claims 16-25 under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps.

Response to Amendment

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

3. Claims 16-17 and 20-24 are rejected under 35 U.S.C. 102(b) as being anticipated by Boggs et al., (US Patent 5,883,074).

Claim 16 is drawn to a method for identifying compounds that modulate resistance to an antibiotic that affects peptidoglycan synthesis in a bacterium comprising: contacting a Beta-lactam-358 (BLR) polypeptide with a test compound; determining the ability of the test compound to modulate an activity of a BLR polypeptide as compared to the activity in the absence of the compound, wherein the ability of the compound to modulate the activity of a BRL polypeptide indicates that the test compound modulates resistance to an antibiotic that affects peptidoglycan synthesis; and selecting those compounds that modulate the activity of the BLR polypeptide to thereby identify compounds that modulate resistance to an antibiotic that affects peptidoglycan synthesis. Claim 17 is drawn to the BLR polypeptide being present in a bacterial cell. Claim 20 is drawn to the method comprises measuring the affect of the test compound on the ability of the bacterial cell to grow in the presence of an antibiotic that affects peptidoglycan synthesis.

Claim 21 is drawn to the antibiotic that affects peptidoglycan synthesis being beta lactam. Claim 22 is drawn to the method comprising measuring the efflux of the test compound or a marker compound from the cell. Claim 23 is drawn to the method wherein the BLR polypeptide is contacted with the test compound *in vitro* and the ability of the test compound to bind to the BLR polypeptide is determined. Claim 24 is drawn to a method for identifying compounds that modulate resistance to an antibiotic that affects peptidoglycan synthesis in a bacterium comprising: contacting an isolated BLR nucleic

acid molecule with a test compound; determining the ability of the test compound to bind to the isolated BLR nucleic acid molecule, wherein the ability of the compound to bind the BRL nucleic acid molecule indicates that the test compound modulates resistance to an antibiotic that affects peptidoglycan synthesis; and selecting those compounds that bind to the BLR nucleic acid molecule to thereby identify compounds that modulate resistance to an antibiotic that affects peptidoglycan synthesis.

Boggs et al., teach methods of screening for compounds that potentiate the activity of antibacterial agents against bacteria. Boggs et al., teach a contact step through the growth of the bacteria in the presence of a Beta-lactam-358 (BLR) polypeptide such as methicillin and various test compounds (col. 12, lines 9-10); determining the ability of the test compound to modulate an activity of a BLR polypeptide as compared to the activity in the absence of the compound (col.12 ,lines 18-22), wherein the ability of the compound to modulate the activity of a BRL polypeptide indicates that the test compound modulates resistance to an antibiotic that affects peptidoglycan synthesis (col. 12 ,lines 31-36); and selecting those compounds that modulate the activity of the BLR polypeptide to thereby identify compounds that modulate resistance to an antibiotic that affects peptidoglycan synthesis (col. 12, lines 40-55). Bogg et al., teach that Beta-lactams inhibit bacterial peptidoglycan synthesis, and are highly effective to treat bacterial infections (col. 1 lines 50-54). It is well known that methicillin is a narrow spectrum Beta-lactam antibiotic and is insensitive to B lactamase activity. The instant specification at page 6 defines Beta-lactam-358 (BLR) polypeptides are those which share a BLR activity including the ability to promote drug

resistance in a cell and do not possess B lactamase activity and therefore include methicillin. Boggs et al., teach potentiation screening assays determine whether or not a test compound such as unknown pharmacological, enhance the ability of the antibacterial agent to stop bacterial growth using high throughput whole cell assays (col. 11 lines 59-65). Boggs et al., also teach *in vitro* application of potentiator assays (col. 15 lines 48-50).

Therefore the BLP polypeptide of the instant specification and the polypeptide of the prior art are equivalent. The prior art peptide appears to possess the same or similar functional characteristics. Since the Patent Office does not have the facilities for examining and comparing applicants' method with the method of the prior art reference, the burden is upon the applicants to show an unobvious distinction between the material structural and functional characteristics of the claimed method of the prior art. See In re Best, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977) and In re Fitzgerald et al., 205 USPQ 594.

Therefore Boggs et al., teach the invention as claimed.

Response to Arguments

4. Applicants' arguments filed September 4, 2003 have been fully considered but they are not persuasive.

5. Applicants argue that Boggs et al., do not teach BLR molecules in a screening assay to identify compounds that modulate resistance to antibiotics that affect

peptidoglycan synthesis in a bacterium. However, Boggs et al., teach contacting step a Beta-lactam-358 (BLR) polypeptide (methicillin) and test compounds. Boggs et al., teach identifying these compounds as modulators or potentaitors of activity. Boggs et al, teach the compounds are screened for intrinsic antibacterial activity. Boggs et al., teach compounds that show no or slight modulation of activity but repress growth as considered potentiators of B-lactam agents. Boggs et al., teach that potentiators enhances the antibacterial effect of an antibacterial agent when the two are used in combination. Therefore, Boggs et al., teach identifying compounds that modulate resistance to antibiotics, because the family of Beta-lactam antibiotics affect peptidoglycan synthesis in a bacterium. Therefore applicants' arguments are not persuasive and the rejection is maintained.

New Grounds of Rejection

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. Claims 16-25 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to

one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a new matter rejection.

Claims 16-25 are drawn to a method for identifying compounds that modulate resistance to an antibiotic that affects peptidoglycan synthesis in a bacterium comprising: contacting a Beta-lactam-358 (BLR) polypeptide with a test compound; determining the ability of the test compound to modulate an activity of a BLR polypeptide as compared to the activity in the absence of the compound, wherein the ability of the compound to modulate the activity of a BRL polypeptide indicates that the test compound modulates resistance to an antibiotic that affects peptidoglycan synthesis; and selecting those compounds that modulate the activity of the BLR polypeptide to thereby identify compounds that modulate resistance to an antibiotic that affects peptidoglycan synthesis.

The claims encompass determining the ability of the compound to modulate the activity of a BRL polypeptide indicates that the test compound modulates resistance to an antibiotic that affects peptidoglycan synthesis, however applicants have not described such a method. The instant specification fails to provide a method wherein every modulation of activity of the BRL polypeptide indicates that the test compound automatically modulates resistance to an antibiotic that affects peptidoglycan synthesis. Neither the specification nor originally presented claims provides support for a method that comprises the ability of the compound to modulate the activity of a BRL polypeptide indicates that the test compound modulates resistance to an antibiotic that affects peptidoglycan synthesis.

Applicant did not point to support in the specification for the ability of the compound to modulate the activity of a BRL polypeptide indicates that the test compound modulates resistance to an antibiotic that affects peptidoglycan synthesis. Thus, there appears to be no teaching of the ability of the compound to modulate the activity of a BRL polypeptide indicates that the test compound modulates resistance to an antibiotic that affects peptidoglycan synthesis. Applicant has pointed to pages 1, 16 and 55-58 of the instant specification and claims for support of the amendment.

However page 1 is drawn to a 358 base pair sequence encoding a novel membrane protein that affects susceptibility to antibiotics that inhibit peptidoglycan synthesis, not to a method for identifying compounds that modulate resistance to an antibiotic that affects peptidoglycan synthesis in a bacterium. Page 16 is drawn to the definition of "specifically" with reference to binding, recognition or reactivity of antibodies including antibodies that bind to a naturally occurring BLR molecule, but are substantially unreactive with other unrelated molecules. Pages 55-68 are drawn to compounds for screening in assays. Therefore, it appears that there is no support in the specification. Therefore, applicants must specifically point to page and line number support for the identity of a method for identifying compounds that modulate resistance to an antibiotic that affects peptidoglycan synthesis in a bacterium comprising: contacting a Beta-lactam-358 (BLR) polypeptide with a test compound; determining the ability of the test compound to modulate an activity of a BLR polypeptide as compared to the activity in the absence of the compound, wherein the ability of the compound to modulate the activity of a BRL polypeptide indicates that the test compound modulates

resistance to an antibiotic that affects peptidoglycan synthesis; and selecting those compounds that modulate the activity of the BLR polypeptide to thereby identify compounds that modulate resistance to an antibiotic that affects peptidoglycan synthesis. Therefore, the claims incorporate new matter and are accordingly rejected.

Conclusion

7. No claims allowed.

8. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

9. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ja-Na Hines whose telephone number is 571-272-0859. The examiner can normally be reached on Monday-Thursday and alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor Bruce Campell, can be reached on 571-272-0974. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Ja-Na Hines
October 30, 2007

MARK NAVARRO
PRIMARY EXAMINER